

In the Claims

Claim 1-3 (Cancelled)

Claim 4 (Previously amended):

A method of producing neural cells from umbilical cord blood comprising:

- (a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells; and
- (b) growing said mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural.

Claim 5 (Previously amended):

The method according to claim 4, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 6 (Previously amended):

The method according to claim 4, wherein said differentiation agent is a mixture of retinoic acid and NGF.

Claim 7 (Previously amended):

The method according to claim 5, wherein said differentiation agent comprises fetal or mature neuronal cells selected from the group consisting of mesencephalic cells and striatal cells.

Claim 8 (Previously amended):

A method of producing neural cells from umbilical cord blood comprising:

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(a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells;

(b) selecting for and isolating said pluripotent stem or progenitor cells within said sample of mononuclear cells; and

(c) growing said stem or progenitor cells from step (b) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural.

Claim 9 (Previously amended):

The method according to claim 8, wherein said selecting and isolating step (b) is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 10 (Previously amended):

1) The method according to claim 8, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 11 (Previously amended):

A method of producing neural cells from umbilical cord blood comprising:

(a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells;

(b) growing said mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said pluripotent stem or progenitor cells within said sample of mononuclear cells to neural; and

(c) selecting for and isolating said neural cells from said pluripotent stem or progenitor cells within said sample of mononuclear cells by essentially eliminating from said sample mononuclear cells having a CD marker.

Claim 12 (Previously amended):

The method according to claim 11, wherein said selecting and isolating step (c) is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 13 (Previously amended):

The method according to claim 11, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 14 (Previously amended):

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The method according to claim 13, wherein said differentiation agent comprises fetal or mature neuronal cells selected from the group consisting of mesencephalic cells and striatal cells.

Claim 15 (Currently amended):

A method of producing a sample of enriched neural cells from a sample of mononuclear cells obtained from umbilical cord blood comprising:

- (a) subjecting the mononuclear cells to an amount of an anti-proliferative agent effective to eliminate essentially all proliferating cells from said mononuclear cell sample;
- (b) exposing the remaining non-proliferating cells from step (a) to a mitogen to provide a population of differentiated cells and quiescent cells comprising a population of pluripotent stem or progenitor cells; and
- (c) growing said population of said differentiated cells and quiescent cells from step (b) to selectively grow said quiescent cells to the essential exclusion of said differentiated cells.

Claim 16 (Previously amended):

The method according to claim 15, comprising the further step of incubating a cell population

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obtained from step (c) to a differentiation agent effective to induce a neural phenotype in said pluripotent stem or progenitor cells.

Claim 17 (Previously amended):

The method according to claim 15, wherein said anti-proliferative agent is Ara-C.

Claim 18 (Previously amended):

The method according to claim 15, wherein said mitogen is selected from the group consisting of epidermal growth factor and pokeweed mitogen.

Claim 19 (Previously amended):

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The method according to claim 16, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 20 (Previously amended):

The method according to claim 19, wherein said differentiation agent is a retinoic acid selected from the group consisting of 9-cis retinoic acid, all transretinoic acid, and a mixture thereof.

Claims 21-42 (Cancelled)

Claim 43 (Previously amended):

A composition comprising umbilical cord blood or a mononuclear cell fraction, thereof, in combination with an effective amount of at least one neural differentiation agent, wherein said umbilical cord blood or mononuclear cell fraction comprise pluripotent stem or progenitor cells, and wherein said amount of neural differentiation agent is effective to induce a neural phenotype in said pluripotent stem or progenitor cells.

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The composition according to ~~claim 40~~ claim 43, further comprising a cell medium to which said differentiation agent is added.

Claim 45 (Currently amended):

3) *ant*
The composition according to ~~claim 40~~ claim 43, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature mesencephalic or striatal cells, brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), nerve growth factor (NGF), fibroblast growth factor (FGF), transforming growth factors (TGF), ciliary neurotrophic factor (CNTF), bone-morphogenetic proteins (BMP), leukemia inhibitory factor (LIF), glial growth factor (GGF), tumor necrosis factors (TNF), interferon, insulin-like growth factors (IGF), colony stimulating factors (CSF), KIT receptor stem cell factor (KIT-SCF), interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, glial-cell missing silencer factor, neuron restrictive silencer factor, SRC-homology-2-domain-containing transforming protein, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 46 (Currently amended):

The composition according to ~~claim 40~~ claim 43, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature mesencephalic or striatal cells, brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), nerve growth factor (NGF), and mixtures thereof.

Claim 47 (Currently amended):

The composition according to ~~claim 40~~ claim 43, wherein said differentiation agent is selected from the group consisting of mixtures of retinoic acid, brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), and nerve growth factor (NGF).

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The composition according to ~~claim 44~~ claim 45, further comprising a cell medium to which said differentiation agent is added.

Claim 49 (Currently amended):

The composition according to ~~claim 40~~ claim 43, wherein said differentiation agent is a mixture of retinoic acid and nerve growth factor.

Claim 50 (Previously amended):

A method of producing a pharmaceutical composition comprising a sample of mononuclear cells being enriched with cells having a neural phenotype marker, said method comprising:

- (a) obtaining a sample of mononuclear cells from umbilical cord blood, wherein said mononuclear cells comprise stem or progenitor cells; and
- (b) growing said mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural; and
- (c) combining said cells obtained from step (b) with a pharmaceutically acceptable carrier, additive or excipient.

Claim 51 (Previously amended):

The method according to claim 50, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 52 (Previously amended):

The method according to claim 50, wherein said differentiation agent is a mixture of retinoic

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acid and NGF.

Claim 53 (Previously amended):

The method according to claim 51, wherein said neuronal cells are selected from the group consisting of mesencephalic cells and striatal cells.

Claim 54 (Currently amended):

A method of producing a pharmaceutical composition comprising neural cells obtained from umbilical cord blood comprising:

(a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise stem or progenitor cells;

(b) selecting for and isolating said pluripotent stem or progenitor cells within said sample of mononuclear cells;

(c) growing said stem or progenitor cells from step (b) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to ~~neural~~ neural; and

(d) combining said cells obtained from step (c) with a pharmaceutically acceptable carrier, additive or excipient.

Claim 55 (Previously amended):

The method according to claim 54, wherein said selecting and isolating step (b) is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 56 (Previously amended):

The method according to claim 54, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

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A method of producing a pharmaceutical composition comprising neural cells obtained from umbilical cord blood comprising:

(a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells;

(b) growing said mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said pluripotent stem or progenitor cells within said sample of mononuclear cells to neural; and

(c) selecting for and isolating said cells having a neural phenotype from said pluripotent stem or progenitor cells within said sample by essentially eliminating from said sample mononuclear cells having a CD marker; and

(d) combining said cells having a neural phenotype isolated from step (c) with a pharmaceutically acceptable carrier, additive or excipient.

Claim 58 (Previously amended):

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The method according to claim 57, wherein said selecting and isolating step c is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 59 (Previously amended):

The method according to claim 57, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, silencers, SHC, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 60 (Previously amended):

The method according to claim 57, wherein said differentiation agent is a mixture of retinoic acid and nerve growth factor.

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The method according to claim 57, wherein said cells having a neural phenotype are selected from the group consisting of mesencephalic cells and striatal cells.

Claims 62-69 (Cancelled)Claim 70 (Previously added):

A method of producing neural cells, said method comprising exposing pluripotent stem or progenitor cells obtained from umbilical cord blood to an amount of a differentiation agent that is effective for changing the phenotype of said stem or progenitor cells to a neural phenotype.

Claim 71 (Previously added):

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The method of claim 70, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature mesencephalic or striatal cells brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), nerve growth factor (NGF), fibroblast growth factor (FGF), transforming growth factors (TGF), ciliary neurotrophic factor (CNTF), bone-morphogenetic proteins (BMP), leukemia inhibitory factor (LIF), glial growth factor (GGF), tumor necrosis factors (TNF), interferon, insulin-like growth factors (IGF), colony stimulating factors (CSF), KIT receptor stem cell factor (KIT-SCF), interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, glial-cell missing silencer factor, neuron restrictive silencer factor, SRC-homology-2-domain-containing transforming protein, proteoglycans, glycoproteins, neural adhesion molecules, and mixtures thereof.

Claim 72 (Previously added):

An isolated neural cell obtainable from umbilical cord blood, wherein said neural cell exhibits both an increase in expression of genes associated with neurogenesis and a decrease in expression of genes associated with hematopoiesis when said neural cell is in the presence of an effective amount of a differentiation agent.

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The isolated neural cell of claim 72, wherein said genes associated with neurogenesis are selected from the group consisting of neurite outgrowth promoting protein, glypican-4, β -tubulin folding cofactor D, pro-galanin, FE65 stat-like protein, glial acidic fibrillary protein, neuron derived orphan receptor, neuronal pentraxin II, neuronal growth protein 43, neuronal PAS1, neuronal DHP-sensitive, voltage-dependent, calcium channel alpha-1D subunit, bone morphogenetic protein 1, retinal glutamate transporter EAAT5, TrkC, ENO2 gene for neuron specific (gamma) enolase, human brain protein recognized by the sera of patients with paraneoplastic sensory neuronopathy, bone morphogenetic protein 2A, neuronal PAS2, survival motor neuron pseudogene, glial growth factor 2, neural cell adhesion molecule Exon SEC, follistatin-related protein, microtubule-associated protein 2, vesicular acetylcholine transporter, neurofilament subunit M, neurofilament subunit NF-L, musashil, bone morphogenetic protein 11, and tenascin-C; and wherein said genes associated with hematopoiesis are selected from the group consisting of HLA class I locus C heavy chain, macrophage receptor MARCO, attractin, alpha-1 collagen type II, leucocyte immunoglobulin-like receptor-8, thymocyte antigen CD1c, erythropoietin receptor, erythropoietin, monocyte chemotactic protein-2, LAG-3 mRNA for CD4-related protein involved in lymphocyte activation, interleukin-7 receptor, complement receptor type 1, T cell receptor, p50-NF-kappa B homolog, lymphocyte-specific protein tyrosine kinase, LAG-3 mRNA for CD4-related protein involved in lymphocyte activation, erythrocyte membrane protein Rh30A, erythrocyte membrane protein band 4.2, leucocyte IgG receptor, and erythroblast macrophage protein.

Claim 74 (Previously added):

The isolated neural cell of claim 72, wherein said neural cell is a human cell.

Claim 75 (Previously added):

The isolated neural cell of claim 72, wherein said neural cell is not a hematopoietic stem cell.

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The isolated neural of claim 72, wherein said neural cell does not express CD34 antigen.

Claim 77 (Previously added):

The isolated neural cell of claim 72, wherein said neural cell is a multipotent neural progenitor cell.

Claim 78 (Previously added):

The isolated neural cell of claim 72, wherein said neural cell differentiates into neurons and glial cells *in vivo*.

Claim 79 (Previously added):

The isolated neural cell of claim 72, wherein said neural cell differentiates into neurons and glial cells in the presence of an effective amount of a differentiation agent.

Claim 80 (Previously added):

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The isolated neural cell of claim 72, wherein said neural cell has been transduced with a polynucleotide that is expressed in said cell.

Claim 81 (Previously added):

An isolated human multipotent neural progenitor cell obtainable from umbilical cord blood, wherein said neural progenitor cell exhibits both an increase in the expression of genes associated with neurogenesis and a decrease in the expression of genes associated with hematopoiesis when said neural progenitor cell is in the presence of an effective amount of a differentiation agent.

Claim 82 (Previously added):

The neural cells produced according to claim 4.

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Claim 83 (Previously added):

The neural cells produced according to claim 8.

Claim 84 (Previously added):

The neural cells produced according to claim 11.

Claim 85 (Previously added):

The sample of enriched neural cells produced according to claim 15.

Claim 86 (Previously added):

The pharmaceutical composition produced according to claim 50.